Effect of inoculum density on human-induced pluripotent stem cell expansion in 3D bioreactors.

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Public Summary:
This paper describes the significance of initial cell number using an interwoven-type hollow fiber based 3D bioreactor.

Scientific Abstract:
OBJECTIVE: For optimized expansion of human-induced pluripotent stem cells (hiPSCs) with regards to clinical applications, we investigated the influence of the inoculum density on the expansion procedure in 3D hollow-fibre bioreactors. MATERIALS AND METHODS: Analytical-scale bioreactors with a cell compartment volume of 3 mL or a large-scale bioreactor with a cell compartment volume of 17 mL were used and inoculated with either 10 x 10(6) or 50 x 10(6) hiPSCs. Cells were cultured in bioreactors over 15 days; daily measurements of biochemical parameters were performed. At the end of the experiment, the CellTiter-Blue((R)) Assay was used for culture activity evaluation and cell quantification. Also, cell compartment sections were removed for gene expression and immunohistochemistry analysis. RESULTS: The results revealed significantly higher values for cell metabolism, cell activity and cell yields when using the higher inoculation number, but also a more distinct differentiation. As large inoculation numbers require cost and time-extensive pre-expansion, low inoculation numbers may be used preferably for long-term expansion of hiPSCs. Expansion of hiPSCs in the large-scale bioreactor led to a successful production of 5.4 x 10(9) hiPSCs, thereby achieving sufficient cell amounts for clinical applications. CONCLUSIONS: In conclusion, the results show a significant effect of the inoculum density on cell expansion, differentiation and production of hiPSCs, emphasizing the importance of the inoculum density for downstream applications of hiPSCs. Furthermore, the bioreactor technology was successfully applied for controlled and scalable production of hiPSCs for clinical use.